Specification

On page 1, please replace the title with the following:

-- A MICROELECTRONIC DEVICE FOR ELECTROCHEMICAL DETECTION OF NUCLEIC ACID HYBRIDIZATION --

Please delete the first two paragraphs of the specification, referred to as "first paragraph A" and "first paragraph B" on page 2 of the Official Action. Please insert the following paragraph after the title:

-- Cross-Reference to Related Applications

This application is a Divisional application of application Serial No. 09/603,217 filed June 26, 2000, now U.S. Patent No. 6,361,951, which is a Divisional application of application Serial No. 09/179,665 filed October 27, 1998, now U.S. Patent No. 6,132,971, which is a Divisional application of application Serial No. 08/667,338 filed June 20, 1996, now U.S. Patent No. 5,871,918, which in turn is a Continuation-In-Part of provisional application Serial No. 60/016,265, filed April 19, 1996 and which claims priority from application Serial No. 08/495,817, filed June 27, 1995 (converted to provisional application Serial No. 60/060,949, filed June 27, 1995), the disclosures of all of which are incorporated by reference herein in their entirety. --

Please replace the paragraph on page 5, lines 1–9 with the following:

-- **Figure 2** shows the cyclic voltammograms of $Ru(bpy)_3^{2+}$ in the presence of 5'-AAATATAGTATAAAA **(SEQ ID NO: 1)** as a single strand (C) and hybridized to complementary strands (A & B). The scan rate is 25 mV/s. (A) represents 25 μM $Ru(bpy)_3^{2+}$ + 100 μM (in guanine nucleotides) double stranded fully hybridized DNA (5'-AAATATAGTATAAAA, **SEQ ID NO: 1**)•(3'-TTTATATCATATTTT, **SEQ ID NO: 2**). (B) represents $Ru(bpy)_3^{2+}$ with a duplex containing a GA mismatch (5'-AAATATAGTATAAAA, **SEQ ID NO: 1**)•(3'-TTTATATAATATTTT, **SEQ ID NO: 3**), and (C) represents $Ru(bpy)_3^{2+}$ a

single strand containing one guanine nucleotide (5'-AAATATAGTATAAAA, **SEQ ID NO: 1**). -

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Please replace the paragraph on page 5, lines15–21 with the following:

Figure 5 shows the cyclic voltammograms of $Ru(bpy)_3^{2+}$ (25 μM) at a scan rate of 25 mV/s in 50 mM sodium phosphate buffer with 0.7 M NaCl, pH 7. (A) No added oligonucleotide. (B) With 75 μM d[5'-TTTTATACTATATTT, **SEQ ID NO: 2**]. (C) With 75 μM of the hybrid of the oligomer from B and d[5'-GGGAAATATAGTATAAAAGGG, **SEQ ID NO: 4**]. Working electrode: tin-doped indium oxide. Reference electrode: Ag/AgCl. Counter electrode: Pt wire. The secondary structure of the hybrid from C is indicated on the Figure.

Please replace the paragraphs on page 6, lines17–26 with the following:

Figure 14 shows the cyclic voltammogram of $Ru(bpy)_3^{2+}$(25 μM) alone and with (100 μM in strands) of 5'-AAATATAG$_n$TATAAAA **(SEQ ID NO: 5)** where n = 1 (G), 2 (GG), or 3 (GGG). The scan rate is 25 mV/s.

Figure 15 shows the cyclic voltammogram of $Ru(bpy)_3^{2+}$ (25 μM) alone and with (100 μM in strands) of 5'-AAATAT(AGT)$_n$ATAAAA **(SEQ ID NO: 6)** where n = 1, 2, or 3. The scan rate is 25 mV/s.

Figure 16 shows the cyclic voltammogram of 25 μM Ruthenium (4,4'-dimethylbipyridine)$_3^{2+}$ (or "$Ru(4,4'\text{-}Me_2\text{-}bpy)_3^{2+}$") alone (solid) and with (100 μM in strands) of 5'-AAATATAGTATAAAA (**SEQ ID NO: 1**, dotted) and 5'-AAATATAGGGTATAAAA (**SEQ ID NO: 5**, dashed). The scan rate is 25 mV/s.

Please replace Table 1 starting on page 37, line 18 with the following:

Table 1. Rate Constants for Oxidation of Guanine in DNA Oligomers by $Ru(bpy)_3^{2+}$

$k(M^{-1} s^{-1})^a$	oligomer sequence	$\Delta r_{Ru-G}(Å)^b$
1.2×10^3	(5'-AAATATAGTATAAAA, **SEQ ID NO: 1**) • (3'-TTTATATCATATTTT, **SEQ ID NO: 2**) GC pair	1.7 Å
5.1×10^3	(5'-AAATATAGTATAAAA, **SEQ ID NO: 1**) • (3'-TTTATATTATATTTT, **SEQ ID NO: 7**) GT mismatch	1.2 Å
1.0×10^{4c}	(5'-AAATATAGTATAAAA, **SEQ ID NO: 1**) • (3'-TTTATATGATATTTT, **SEQ ID NO: 8**) GG mismatch	1.0 Å
1.9×10^4	(5'-AAATATAGTATAAAA, **SEQ ID NO: 1**) • (3'-TTTATATAATATTTT, **SEQ ID NO: 3**) GA mismatch	0.7 Å
1.8×10^5	(5'-AAATATAGTATAAAA, **SEQ ID NO: 1**) single strand	0 Å
5.1×10^3	(5'-AAATATAGTATAAAA, **SEQ ID NO: 1**) • (3'-TTTATATCTATTTT, **SEQ ID NO: 9**)	1.2 Å

[a]DNA concentrations used to determine rate constants were based on the moles of guanine nucleotides. [b]Estimated distance of tunneling through solvent. Distances calculated according to $k/k_{ss}=\exp[-\beta\Delta r]$, where $\beta(H_2O)=3Å^{-1}$ and $k_{ss}=1.8 \times 10^5 M^{-1}s^{-1}$. [c]Since the rate constants are relative to guanine concentrations, the observed rate for the GG mismatch has been normalized relative to the other oligomers containing a single guanine.

Please enter the attached paper copy of the Sequence Listing at the end of the specification.

Attachment: paper copy of Sequence Listing